Natl. Acad. Sci. USA 93: 13902-13907. Similarly, Kruk et al. reported a higher level of telomerase in the early S phase when compared to other points in the cell cycle (Biochem. Biophys. Res. Commun. (1997) 233: 717-722). However, other researchers have reported conflicting results, and have alternatively suggested that telomerase activity correlates with growth rate, not cell cycle (Holt et al. (1996) Mol. Cell. Biol. 16(6): 2932-2939; see also Holt et al. (1997) Proc. Natl. Acad. Sci. USA 94: 10687-92; and Belair et al. (1997) Proc. Natl. Acad. Sci. USA 9: 13677-13682). Still others have proposed that telomerase activation is mediated by other cellular activation signals, as evidenced by the upregulation of telomerase in B cells *in vitro* in response to CD40 antibody/antigen receptor binding and exposure to interleukin-4 (Weng et al. (1997) Proc. Natl. Acad. Sci. USA 94: 10827-32; see also Hiyama et al. (1995) J. Immunol. 155 (8): 3711-3715). But despite the rising interest in telomerase and its purported role in the process of aging and cellular transformation, the regulation of telomerase activity remains poorly understood. See, e.g., Smaglik, "Turning to Telomerase: As Antisense Strategies Emerge, Basic Questions Persist," *The Scientist*, January 18, 1999, 13(2): 8)--

B 1

Please substitute the paragraph beginning at page 8, line 6 with the following amended paragraph:

-- The present invention stems from the discovery that nuclear transfer techniques may be used to extend the life span of senescent or near-senescent cells by activating endogenous (cellular) telomerase activity. This provides particular advantages over recently publicized approaches for resolving the telomere loss seen in nuclear-transfer generated animals, which focus on the exogenous expression of a cloned telomerase gene to resolve telomere shortening in cloned mammals. For instance, researchers at Geron Corporation and the Roslin Institute have recently collaborated to combine Geron's cloned telomerase gene with

B 2

nuclear transfer in order resolve telomere shortening in clones. See, e.g., Business Wire, May 26, 1999. This announcement preceded the May 27th Nature report by researchers at Roslin Institute that two other sheep (after Dolly) cloned by nuclear transfer also exhibit shorter telomeres than age-matched controls. Researchers at the University of Massachusetts involved in cloning cattle also believed that transfecting donor cells with an exogenous telomerase gene might be beneficial for the lifespan of cloned animals, despite the observation that nuclear transfer seemed to rejuvenate senescent donor cells. ABC News (Reuters), Daily News, May 22, 1998.--

B2

Please replace the paragraph beginning at page 26, line 13 with the following amended paragraph:

-- For instance, Xu et al. demonstrated that re-expression of the retinoblastoma protein in tumor cells induces senescence and inhibits telomerase activity (Oncogene (1997) 15: 2589-2596). A recent report also suggests that a gene on chromosome 3 may be involved in transcriptional repression of hTERT, the catalytic subunit of telomerase. See Horikawa et al. (1998) Mol. Carcinog. 22(2): 65-72. Several proteins have also been identified that interact directly with telomerase, such as p23/hsp90 (molecular chaperones) and TEP1 (telomerase associated protein 1). Id. Researchers at Lawrence Berkeley National Laboratory have purported cloned two additional human telomere-associated proteins (Tin 1 and Tin 2). Federal Technology Report, December 30, 1999, Partnership Digest, Technology Watch, p. 9. Thus, the regulatory mechanism identified by the present methods could operate by binding to or inhibiting the expression of a telomerase binding protein or a telomerase repressor, consequently increasing telomerase activity, but could also regulate telomerase activity by upregulating gene expression or enhancing protein stability. --

B3